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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,059	12/14/2005	William Marshall Stark	056646-5024	2559

9629 7590 08/11/2009
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EXAMINER

CHOWDHURY, IQBAL HOSSAIN

ART UNIT	PAPER NUMBER
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1652

MAIL DATE	DELIVERY MODE
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08/11/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/529,059	Applicant(s) STARK ET AL.	
	Examiner IQBAL H. CHOWDHURY	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4,46,47,52,54,57-59 and 67 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 4 is/are allowed.
- 6) ☒ Claim(s) 46,47,52,54,57-59 and 67 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>6/15/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Application Status

Claims 4, 46-47, 52, 54, 57-59 and 67 are currently pending in this application.

In response to a previous Office action, an Examiner's amendment (mailed on May 1, 2009), Applicants filing of an IDS on June 15, 2009 is acknowledged.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 15, 2009 has been entered.

Claims 4, 46-47, 52, 54, 57-59 and 67 are under consideration.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 15, 2009 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is considered by the examiner. The signed copy of 1449 is enclosed herewith.

Claim objection

Claim 54 is objected to because of the following informalities:

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Claim 54 is objected to in the recitation "2,3 interface further comprising R2A and E56K" (see previous office action, Ex. Amendment, mailed on 5/1/2009), which should be "2,3 interface are R2A and E56K". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46-47, 52, 54, 57-59 and 67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. .The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner acknowledges that the withdrawal of the rejection in an office action mailed on 2/17/2009 was an error.

Claims 46-47, 52, 54, 57-59 and 67 are directed to a genus of a serine recombinase comprising a catalytic domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of TN3 resolvase of SEQ ID NO: 2, wherein said serine recombinase comprises any one or more mutations of the surface residues corresponding to a 2'3 interface and said catalytic domain contains (comprises) any one or more additional mutations at a position selected from the group consisting of V107, A117, A89, F92, L66, G70, M76, T109, and R121 or any one or

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more additional mutations at said positions corresponding to TN3 resolvase of SEQ ID NO: 2.

The claims still read on a catalytic domain of serine recombinase comprising any one or more mutations of the surface residues corresponding to a 2'3 interface and a catalytic domain comprising any one or more additional mutations of said positions in a catalytic domain recited in claim 46 (and dependent claims), wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of TN3 resolvase of SEQ ID NO: 2. The serine recombinase comprising any one or more mutations of the surface residues corresponding to a 2'3 interface and the catalytic domain of serine recombinase comprising any one or more additional mutations at a position selected from the group consisting of V107, A117, A89, F92, L66, G70, M76, T109, and R121 or any one or more additional mutations at said positions corresponding to TN3 resolvase of SEQ ID NO: 2 renders the catalytic domain of serine recombinase having no structure, i.e. the recitation of "one or more additional mutations" as well as "one or more mutations" of the surface residues of 2,3 interface, which interpret unlimited number of mutations that makes the protein having no structural feature.

As discussed in the written description guidelines the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

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identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A representative number of species means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. Satisfactory disclosure of a representative number depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of species disclosed. For inventions in an unpredictable art, adequate written description of a genus, which embraces widely variant species, cannot be achieved by disclosing only one species within the genus. The specification teaches few representative species of SEQ ID NO: 2 and few modifications. The genus of polypeptide of a serine recombinase is structurally diverse as it broadly encompasses many variants comprising recombinase activity having different structures. Therefore, disclosing similar modifications would not be sufficient to describe the claimed invention, which also encompasses many other mutations at the same time nor are the claims limited to making the mutations in serine recombinases having the specific characteristics, i.e. having common identity of amino acid residues among different serine recombinases or serine recombinases known in the art nor are the mutant enzymes that are made required to have these characteristics. As such, the disclosure solely of functional features coupled with minor structural feature, present in all members of the genus is insufficient to be representative of the attributes and features of the entire genus.

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Arguments:

Applicants did not have any arguments in the response filed on 01/12/2009 except mentioning that claims 1-2, 5-45, 48-51, 53, 60-66 and 68-69 are canceled or remaining claims are amended by adding limitation from the previously examined claims.

Response:

Applicants arguments filed on 1/12/2009 have been fully considered but are not found persuasive because canceling claims 1-2, 5-45, 48-51, 53; 60-66 and 68-69 do not affect the limitation in independent claim 46 and dependent claims thereof. The issues raised by the Examiner are still present in claim 46 and dependent claims.

Claims 46-47, 52, 54, 57-59 and 67 are rejected under 35 U.S.C. 112, first paragraph on scope of enablement. . The Examiner acknowledges that the withdrawal of the rejection in an office action mailed on 2/17/2009 was an error.

The specification, while being enabling for a serine recombinase Tn3 resolvase of SEQ ID NO: 2 from E. coli comprising a catalytic domain and a DNA binding domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of Tn3 resolvase of SEQ ID NO: 2, wherein said serine recombinase contains additional mutations at positions selected from the group consisting of L105, V107, A117, A89, F92, L66, G70, M76, T109, and R121 or at said positions corresponding to TN3 resolvase of SEQ ID NO: 2, does not reasonably provide enablement for a serine

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recombinase comprising any one or more mutations of the surface residues corresponding to a 2'3 interface and a catalytic domain of a serine recombinase having a mutation G101S and any number of additional mutations in the recitation of " contains (comprises) one or more additional mutations" including the mutations at the recited positions or at a position corresponding to G101 and positions V107, A117, A89, F92, L66, G70, M76, T109, and R12 of a Tn3 resolvase of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Arguments:

Applicants did not have any arguments in the response filed on 01/12/2009 except mentioning that claims 1-2, 5-45, 48-51, 53, 60-66 and 68-69 are canceled or remaining claims are amended by adding limitation from the previously examined claims.

Response:

Applicants arguments filed on 1/12/2009 have been fully considered but are not found persuasive because canceling claims 1-2, 5-45, 48-51, 53; 60-66 and 68-69 do not affect the limitations in independent claim 46 and dependent claims. The issues raised by the Examiner are still present in claim 46 and dependent claims.

Applicants arguments have been fully considered but are not deemed persuasive to overcome the rejection on scope of enablement issues. The claims still read on a

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serine recombinase comprising any one or more mutations of the surface residues corresponding to a 2'3 interface and a catalytic domain of a serine recombinase comprising a mutation of G101 and any one or more additional mutations at recited positions such as V107, A117, A89, F92, L66, G70, M76, T109, and R12 corresponding to TN3 resolvase of SEQ ID NO: 2. Since, serine recombinases are diverse which encompass many mutations; one of ordinary skilled in the art would not know how to make the claimed mutant protein from the guidance of TN3 resolvase of SEQ ID NO: 2, which require undue experimentation.

Claims 46-47, 52, 54, 57-59 and 67 are substantial broad in the context of the recitation of "one or more mutations of the surface residues corresponding to a 2'3 interface" and "one or more additional mutations at recited positions corresponding to TN3 resolvase of SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the substantially large number of serine recombinases broadly encompassed by the claims.

Claims 46-47, 52, 54, 57-59, and 67 are broadly drawn to a serine recombinase comprising one or mutations of the surface residues corresponding to a 2'3 interface and a catalytic domain of serine recombinase comprising any one or more additional mutations at said positions corresponding to TN3 resolvase of SEQ ID NO: 2. Claims do not specify any specific sequence due to the recitation of "one or mutations of the surface residues corresponding to a 2'3 interface" or "one or more additional mutations, which lacks structural feature. The specification is enabled for serine recombinase of SEQ ID NO: 2 with a mutation at position G101 and corresponding several mutations

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comprising catalytic domain of SEQ ID NO: 2. Also, while the specification may provide some guidance as to which amino acids can be mutated to obtain the desired functional properties if there is a significant level of homology between related serine recombinases, in the instant case, it is unclear as to how the teachings of the specification adequately enabled the mutation of a serine recombinase having one or more additional mutations having claimed functional characteristics.

Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a serine recombinase comprising any one or more mutations of the surface residues corresponding to a 2'3 interface" and a catalytic domain of a serine recombinase comprising a mutation at position G101 and any one or more additional mutations at said positions corresponding to SEQ ID NO: 2 comprising a catalytic domain, wherein said catalytic domain is mutated at G101 or at a position corresponding to G101 of a Tn3 resolvase of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of a modified serine recombinase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

Status of the claims:

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Claims 4, 46-47, 52, 54, 57-59 and 67 are pending.

Claim 4 is allowed.

Claims 46-47, 52, 54, 57-59 and 67 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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